REMARKS

In response to the office communication dated June 1, 2007 which asserted that the previous response (filed March 8, 2007) to the Office Action was not fully responsive because the elected species (SEQ ID NO: 45) did not fall within the genus recited in claim 1, Applicant hereby amends claim 1 to recite the limitation of "13-100 nucleotides". Support for the amendment is found in the specification on page 17 which teaches that the ODN may be in the size range of 13-100 nucleotides. Therefore the elected species (SEQ ID NO: 45) now falls within the genus recited in claim 1. The amendment is consistent with the response filed on March 8, 2007, the entire text of which is repeated below but modified according to the change to claim 1.

Claims 1-37, 52, 63-65, 68-69, and 75 were previously pending in this application. Claim 1 is amended to add the limitation of "13-100 nucleotides". Support for the amendment is found in the specification on page 17 which teaches that the ODN may be in the size range of 13-100 nucleotides. Claims 2-5, 11-16, 20-22, 25-37, 52, 63-65, 68, 69, and 75 are withdrawn. Claim 90 is added. Claims 1, 6-8, 10, 17-19, 23, 24 and 90 are pending for examination with claims 1 and 90 being an independent claim. Support for new claim 90 is found within original claim 1 and in the specification on page 17 which teaches that the ODN may be in the size range of 13-40 nucleotides.

No new matter has been added.

Applicants acknowledge that the Examiner has made the restriction/election requirement FINAL. The Examiner has acknowledged Applicants' election with traverse of Group I, claims 1, 6-10 and 13-24 and a species of X1=A, X2=A and N1=ATTTTTTTTTTA.

Applicants acknowledge that claims 2-5, 11-16, 20-22, 25-37, 52, 63-65, 68, 69 and 75 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected inventions and/or species. However, Applicants acknowledge the indication by the examiner that upon allowance of a generic claim that additional species will be considered.

Claims 1, 6-8, 10, 17-19, 23, 24 and 90 are pending.

Claim Rejections – 35 U.S.C. §112

Claims 1, 6-10, 17-19, 23 and 24 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Examiner alleges that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

The Applicants agree that the claims are directed to oligonucleotides described by the formula in Claim 1 and may contain modified internucleotide linkages. The elected species in particular is described in SEQ ID NO:45; it is a 17-mer of the sequence 5'-TCGAAATTTTTTTTTTA-3'.

The Examiner alleges that neither the specification nor the claims disclose the structure of the oligonucleotide set forth in Claim 1. Applicants respectfully disagree. The description, figures and claims disclose numerous examples of the oligonucleotides set forth in Claim 1, their sequences and structures. The application and the accompanying sequence listing disclose sixty-nine specific examples of oligonucleotides set forth in Claim 1. For example, the elected species of oligonucleotide, SEQ ID NO: 45, is described in the Examples Section, page 49, and furthermore, Figure 9 clearly shows a dose response in production of immunogenic response by SEQ ID NO:45.

The Examiner alleges that the recitation of "comprising" in Claim 1 indicates that there are other structural components to the claimed oligonucleotide. The term comprising is open language which allows the inclusion of other elements beyond the specified elements. However, in claim 1 and the claims dependent thereon specific limits are placed on the 5' and 3' ends of the oligonucleotide. In the structure a 5' and 3' end of the molecule are defined as the ends of the oligonucleotide. In the specification on page 13 it is taught that in the "formulas 5' refers to the free 5' end of the oligonucleotide and 3' refers to the free 3' end of the oligonucleotide." The majority of claims use the open language "comprising" to indicate that other elements may be included. That in itself cannot serve as the basis for a lack of written description requirement, when the other elements of the claims are presented with sufficient specificity.

The Examiner alleges that the claims do not set any function or specific structure for the claimed oligonucleotides. Contrary to Examiner's assertions, the claimed invention is not described solely in terms of methods of its making coupled with its function. There is art-recognized correlation between the structure of the invention and its function. As discussed in the specification, is has been understood and held in the art that immune stimulatory effects of bacterial DNA are a result of the presence of unmethylated CpG dinucleotides in particular base contexts (CpG motifs), which are common in bacterial DNA, but methylated and underrepresented in vertebrate DNA (Krieg et al, 1995 Nature 374:546-549; Krieg, 1999 Biochim. Biophys. Acta 93321:1-10). The immune stimulatory effects of bacterial DNA can be mimicked with synthetic oligodeoxynucleotides containing these CpG motifs. These immune stimulatory effects of native phosphodiester backbone CpG ODN are highly CpG specific in that the effects are dramatically reduced if the CpG motif is methylated, changed to a GpC, or otherwise eliminated or altered (Krieg et al, 1995 Nature 374:546-549; Hartmann et al, 1999 Proc. Natl. Acad. Sci USA 96:9305-10). In early studies, it was thought that the immune stimulatory CpG motif followed the formula purine-purine-CpG-pyrimidine-pyrimidine (Krieg et al, 1995 Nature 374:546-549; Pisetsky, 1996 J. Immunol. 156:421-423; Hacker et al., 1998 EMBO J. 17:6230-6240; Lipford et al, 1998 Trends in Microbiol. 6:496-500). It has now been discovered that oligonucleotides having a '5TCG motif, rather than the conventional hexamer motif, without any additional unmethylated CpG motifs have strong immunostimulatory capability. The instant invention claims the novel structures of such oligonucleotides (ODNs) and their function in stimulating various types of immunogenic responses as illustrated by the examples and drawings of the instant specification.

The biomolecule sequences of the invention are not described merely by functional characteristics. The biomolecule sequences of the invention are described by structure, formula, name, and physical properties – as oligonucleotides with specific sequences, specific lengths, and specific internucleotide linkages. In addition, modifications to the bases, nucleosides, and the linkages as envisaged by the instant invention are also described. The specific sequence requirements, linkages and structures of the oligonucleotides of the instant invention are shown in Table 1 on page 47, and in great detail in the Examples section. In brief, the examples and drawings of the instant specification clearly show that 5'-TCG enhances the immunostimulatory activity of

non-CpG or CpG ODNs as determined by IL-10 and IFN-α production and different cellular effects. 5'-TCG are the most potent and efficient ODNs to induce a strong Th1-mediated immune response. In addition to a 5'-TCG, the length and the sequence of an ODN have an effect on stimulatory activity. As shown in Example 9, IL-10 secretion is induced by ODNs with 5'-TCG and increasing numbers of thymidines and as shown in Example 12, Type I IFN secretion is induced by short 5'-TCG ODNs. As shown in Example 16, modifications of the T preceding the 5'-CG are allowed. Finally, Example 13 summarizes the *in vitro* immune stimulation by a panel of ODNs according to the described observations. Clearly, the specification describes the structures and function of the novel ODNs that comprise the invention.

A skilled artisan can immediately envision the product claimed from the disclosure. A skilled artisan could easily select an appropriate oligonucleotide based on the disclosure that would stimulate the desired immunogenic response. Furthermore, a skilled artisan could easily synthesize and use such a compound because the art of nucleic acid synthesis, formulation and administration is well developed and such a process would not be beyond what is routinely carried out in the art.

The claims are broad but adequately described. The specification describes a representative number of the claimed oligonucleotides as to reasonably convey to the skilled artisan the invention; namely, oligonucleotides having a 5'TCG motif without any additional unmethylated CpG motifs. Further characteristics such as sequence, length and internucleotide linkages are described in detail in the specification as well. The application also includes a sequence listing of about seventy sequences that are representative of the claimed genus and species. Examples of the specific immunostimulatory activity of many of those sequences are included in the Examples and Drawing sections. Therefore, Applicants have clearly demonstrated that at the time of the invention they were in possession of the claimed genus by presenting examples and a specification that shows that the invention was "ready for patenting". Applicants respectfully request that the Examiner withdraws the rejection under first paragraph, 35 U.S.C. §112.

Claim Rejections – 35 U.S.C. §102

Claims 1, 6-10 and 17-19 have been rejected under 35 U.S.C. 102(b) as being anticipated

by Klinman et al. (WO 00/61151; publication date Oct. 19, 2000). Klinman et al. discloses oligonucleotides with SEQ ID NO: 117, 119, 120, 133 and 135 which, according to the Examiner, would be encompassed by the formula claimed in instant Claim 1.

Applicants have amended Claim1 to add the limitation that the oligonucleotide is 13-100 nucleotides in length. Although some of the general language cited in Klinman et al suggest that oligonucleotides can have lengths up to 100 nucleotides, there is no teaching that the oligonucleotides of SEQ ID NO: 117, 119, 120, 133 and 135 have a length between 13 and 100 nucleotides. In fact each has a specified length of 12 nucleotides according to the sequence listing. New claim 90 includes the limitation that the oligonucleotide has a length of 13-40 nucleotides. Therefore, the rejection under 35 U.S.C. 102(b) in view of Klinman et al. (WO 00/61151) should be withdrawn and is not applicable to new claim 90.

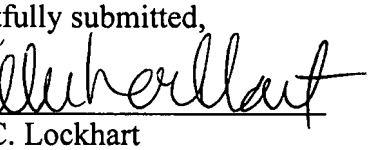
Applicants acknowledge that claims 23 and 24 are not rejected in view of the prior art.

REMARKS

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: July 2, 2007

Respectfully submitted,

By 

Helen C. Lockhart
Registration No.: 39,248
WOLF, GREENFIELD & SACKS, P.C.
Federal Reserve Plaza
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
(617) 646-8000